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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,857	12/11/2003	Michael Patane	CASM122094	8103
26389	7590	10/20/2004	EXAMINER	
CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC			FORD, ALLISON M	
1420 FIFTH AVENUE			ART UNIT	
SUITE 2800			PAPER NUMBER	
SEATTLE, WA 98101-2347			1651	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/733,857

Applicant(s)

PATANE, MICHAEL

Examiner

Allison M Ford

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 17-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-16 is/are rejected.
- 7) ☒ Claim(s) 6 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

Art Unit: 1651

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election without traverse of Group I, claims 1-16, in the reply filed on 09/16/2004 is acknowledged.

### ***Status of Application***

Claims 1-16 are being examined for patentability. Claims 1-20 are pending in the current application, of which 17-20 have been withdrawn from consideration.

### ***Priority***

Acknowledgement is made of applicant's claim for priority to foreign application 2003902303, filed 05/14/2003 in Australia. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### ***Specification***

The disclosure is objected to because of an informal spelling error: Pg. 11, ln 12, should read, "...activity of the crude extract, during the step of heating PDE-1 as described in Example 7."

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: EXTRACTION AND PURIFICATION OF PHOSPHODIESTERASE 1.

Appropriate correction is required.

Art Unit: 1651

***Claim Objections***

Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for purifying PDE-1 from a barley cell including releasing PDE-1 from the cell into a solution including calcium and magnesium to form an extract; and heating the extract up to 65 °C to increase the specific activity of PDE-1, does not reasonably provide enablement for heating the extract to temperatures above 65-70°C. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. At temperatures above 65-70°C the PDE-1 denatures (See Sander et al, *Biochemistry* (1997) Pg. 6103, col. 2; See Specification, Pg 4); therefore, the temperature to which the extract is heated must have an upward limitation below 65-70°C.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless —

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1651

Claims 1, 4, 5, & 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Holle et al (US Patent 3,516,907).

Applicant's claim 1 is directed to a process for purifying a phosphodiesterase 1 (PDE-1) from a cell including heating an extract of a cell formed from a solution including at least one divalent cation, to increase the specific activity of PDE-1 in the extract. Claim 4 requires the concentration of the divalent cation to be less than 100mM. Claim 5 requires the concentration of the divalent cation to be about 10 mM to 50 mM. Claim 7 requires the extract to be heated to a temperature that permits depletion of phosphomonoesterase activity from the extract. Claim 8 requires the extract to be heated to between about 45°C and 75°C. Claim 10 requires the extract to be heated to about 60°C.

Holle et al teach a process for purifying a phosphodiesterase 1 (PDE-1) from crude extract of vegetable cells, including barley cells (See col. 2, ln 49-55), comprising heating an extract of a cell containing 5'-phosphodiesterase (which applicant refers to as PDE-1, See IUMBM Enzyme Nomenclature, EC 3.1.4.1) in a solution containing a heavy metal salt, such as  $\text{ZnCl}_2$ ,  $\text{CuCl}_2$ , and  $\text{MnCl}_2$ , ( $\text{Zn}^{2+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Mn}^{2+}$  being divalent cations) at a temperature between 55 and 65°C (See col. 2, ln 1-15, and col. 10, ln 36-48) (Claims 1 & 7-10). Holle et al teach the concentration of the heavy metal salts to be between 2 mM and 5 mM (See col. 3, ln 46-48); 5 mM is being defined by the examiner to be about 10 mM (Claims 4 & 5). Therefore the reference anticipates the claimed subject matter.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1651

Claims 1-5, 7-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holle et al (US Patent 3,516,907), in view of Harvey et al (*Biochemistry*, 1967) and De-Eknamkul et al (US Patent 5,879,916), and in light of Hsin et al (*Blood*, 1998).

Applicant's claim 1 is directed to a process for purifying a phosphodiesterase 1 (PDE-1) from a cell including heating an extract of a cell formed from a solution including at least one divalent cation, to increase the specific activity of PDE-1 in the extract. Claim 2 requires the divalent cation to be magnesium or calcium. Claim 3 requires the divalent cation to be magnesium and calcium. Claim 4 requires the concentration of the divalent cation is less than 100mM. Claim 5 requires the concentration of the divalent cation to be about 10 mM to 50 mM. Claim 7 requires the extract to be heated to a temperature that permits depletion of phosphomonoesterase activity from the extract. Claim 8 requires the extract to be heated to between about 45°C and 75°C. Claim 10 requires the extract to be heated to about 60°C. Claim 11 is directed to a process for purifying PDE-1 from a barley cell, including releasing PDE-1 from the cell into a solution including calcium and magnesium to form an extract; and heating the extract to increase the specific activity of PDE-1 in the extract. Claim 12 requires the extract to be maintained in conditions for promoting solubilization of the phosphodiesterase in the extract prior to heating the extract. Claim 13 requires the extract to be maintained at less than 10°C. Claim 14 requires the extract to be maintained at temperatures between 0 to about 4°C. Claim 15 requires the further step of chromatography to purify PDE-1 from the heated extract. Claim 16 requires the chromatography to be anion exchange chromatography.

Holle et al teach a process for purifying a phosphodiesterase 1 (PDE-1) from crude extract of vegetable cells, including barley cells (See col. 2, ln 49-55), comprising heating a cell extract containing 5'-phosphodiesterase in a solution containing a heavy metal salt, such as  $\text{ZnCl}_2$ ,  $\text{CuCl}_2$ , and  $\text{MnCl}_2$ , ( $\text{Zn}^{2+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Mn}^{2+}$  being divalent cations) at a temperature between 55 and 65°C (See col. 2, ln 1-15, and col. 10, ln 36-48) (Claims 1 & 7-10). Holle et al teach the concentration of the heavy metal salts to be

Art Unit: 1651

between 2 mM and 5 mM (See col. 3, ln 46-48) (Claim 4). Though Holle et al describe using between 2 mM and 5 mM of heavy metal salts, it would have been obvious to one of ordinary skill in the art to experiment with slightly higher concentrations of metal salts up to and including a concentration of 10 mM (Claim 5). One would be motivated to manipulating the concentration within a reasonable range, such as +/- 5 mM, because the references clearly indicates that the various proportions and amounts of the ingredients used in the claimed composition are result effective variables, they would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references.

Holle et al further purify PDE-1 from the heated barley extract containing divalent cations by running the extract solution on an anion exchange chromatography column, Sephadex DEAE, Type A50 (See col. 5, ln 70- col. 6, ln 9) (Claims 11, 15-16). Holle et al does not explicitly say the Sephadex DEAE, Type A50 is an anion exchange column and Sephadex is no longer an independent company publishing a catalog, however, Hsin et al (*Blood*, 1998) reference use of the Sephadex DEAE, Type A 50 column and do specifically state it is an anion exchange chromatography column (See Hsin et al, Pg 3269, col. 1).

Though Holle et al teach using divalent cations, he does not specifically teach magnesium or calcium. However Harvey et al teach divalent metal ions, such as magnesium and calcium, increase the specific activity of the PDE-1 enzyme, as evidenced by a two-fold increase in specific activity of PDE-1 when used in presence of 2 mM divalent cation (See Harvey et al, Pg. 3692, col. 1, & Table II).

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute magnesium or calcium chloride, for the zinc, copper, and manganese chlorides used by Holle et al. The person of ordinary skill in the art would have been motivated to substitute magnesium or calcium chloride for zinc, copper, and manganese chloride in order to cut back on the toxicity risks of zinc and manganese, or if they had magnesium chloride or calcium chloride more readily available in their laboratory (Claims 2 & 11). One would expect success because they are all divalent cations, and

Art Unit: 1651

Holle et al has taught success using zinc, copper, and manganese, and Harvey et al teach magnesium and calcium also increase the specific activity of PDE-1 (See Holle et al, col. 2, ln 1-15, and col. 10, ln 36-48; & See Harvey et al, Pg. 3692, col. 1, & Table II).

It would have further been obvious to one of ordinary skill in the art at the time the invention was made to add both calcium and magnesium to the extract solution prior to heating, in the method of Holle et al (Claim 3). A person of ordinary skill in the art would have been motivated to add both divalent cations in order to further increase the specific activity. One would have expected success because Harvey et al teach they both increase specific activity of PDE-1 (See Harvey et al, Pg. 3692, col. 1 & Table II), and there is no evidence they counteract one another.

Holle et al do not describe maintaining the extract solution in conditions that would promote solubilization of the phosphodiesterase in the extract prior to heating, their focus was more on heating. However, it is advantageous to maintain the extract solution at low temperatures prior to heating because low temperatures inhibit the action of proteolytic enzymes present in the crude extract (See De-Eknamkul et al). Active proteolytic enzymes could have a negative effect on the desired enzymes. Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to maintain the extract solution at low temperatures prior to heating the extract (Claim 12). De-Eknamkul et al teach maintaining enzymes at 0-10°C, optimally at 4°C to prevent unwanted enzymatic activity during enzyme extraction (See De-Eknamkul et al, col. 3, ln 12-29) (Claims 13 & 14). The person of ordinary skill in the art would have been motivated to maintain the enzymes at temperatures between 0-10°C, optimally at 4°C to allow more time for solubilization and extraction, without the threat of other enzymes in the crude extract acting destructively. One would expect success because De-Eknamkul et al teach temperatures between 0-10°C, optimally 4°C, do prevent the majority of enzyme activity (See col. 3, ln 25-27).

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.



Art Unit: 1651

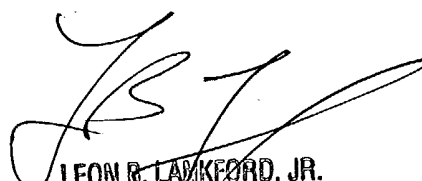
***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M Ford whose telephone number is 571-272-2936. The examiner can normally be reached on M-F 7:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0927. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford  
Examiner  
Art Unit 1651

  
LEON R. LAMKEFORD, JR.  
PRIMARY EXAMINER